

Amendments to the specification:

Please amend the specification starting at page 23, line 20 as follows:

FIGURE 1A: ~~Amino acid~~ Amino acid sequence of tau (SEQ ID NO:1) (isoform htau40, Goedert et al., 1989). The motifs SP, TP, IGS and CGS are highlighted.

Please amend the specification starting at page 24, line 27 as follows:

FIGURE 3: Diagram of constructs K3M, K10, K19, and K17. K19 (99 residues) contains the sequence Q244-E372 (SEQ ID NO: 28) of htau23 plus an N-terminal methionine. This comprises three of the repeats (repeat 1, 3, and 4; repeat 2 is absent in htau23). K10 (168 residues) is similar, except that it extends to the C-terminus of htau23 (L441). K17 (145 residues) contains the sequence S198-E372 (assembly domain starting at the chymotryptic cleavage site, up to end of fourth repeat, but without the second repeat, plus an N-terminal methionine). K3M (335 residues) contains the N-terminal 154 residues of bovine tau4, plus the sequence R221-L441 of htau23 (without second repeat). The location of peptide S198-T220 is indicated in K17. By comparison of the constructs the epitope of AT8 must be in this region (see FIGURE 4).

Please amend the specification starting at page 25, line 32 as follows:

FIGURE 5: Diagram of tryptic peptide S195-R209. The 15 residue peptide (SEQ ID NO: 29) (containing 5 serines and 1 threonine) was labeled with two radioactive phosphates at S199 and S202, as determined by sequencing.

Please amend the specification starting at page 28, line 33 as follows:

FIGURE 10: Diagram of htau40, showing the location of the 7 ser-pro motifs phosphorylated by the kinase activity. The boxes labeled 1-4 are the internal repeats involved in microtubule binding; the second is absent in some isoforms (e.g. htau23). The two shaded boxes near the N-terminus are inserts absent in htau23 and htau24 so that these molecules have only 6 ser-pro motifs. The following radioactive tryptic peptides were found:

24-49: KDQGGYTMHQOQEGOTDAGLKES.PLQ (SEQ ID NO: 31)

191-209: SGDRGYSS.PGS.PGTPGSR (SEQ ID NO: 32)

231-240: TPPKS.PSSAK (SEQ ID NO: 33)

396-405: SPVVSGDTS.PR (SEQ ID NO: 34)

385-405: TDHGAEIVYKS.PVVSGDTS.PR (SEQ ID NO: 35)

407-428: HLSNVSTGSIDMVDS.PQLATL (SEQ ID NO: 36)

260-266: IGS.TENL (SEQ ID NO: 37)

Please amend the specification starting at page 43, line 24 as follows:

FIGURE 41: Diagram of htau40, highlighting the first microtubule-binding repeat (SEQ ID NO: 30) and the Ser262 that is important for microtubule binding.

Please replace the paragraph on page 59, lines 21-32 with the following paragraph:

The major phosphorylated motifs of neurofilaments are repeated sequences of the type KSPV (SEQ ID NO. 38) where S is the phosphate acceptor; see e.g. Geisler et al., FEBS Lett. 221 (1987), 403-407. Tau has one such motif, centered at S396, and another KSP motif is centered at S235. The two KSP sites lie on either side of the repeat region and are conserved in all tau isoforms. By analogy one may suspect that these sites are involved in the reaction with the SMI antibodies that were raised against neurofilaments. We tested this in three ways, by mutating one or two of the serines, by making smaller tau constructs, and by direct sequencing of tryptic peptides.